Multicenter, Open-label, Post-Authorization Safety Study (PASS) of Elsulfavirine (Elpida®) Used In First-line Therapy For HIV-1- Infected Patients Added to Standard ART (NNRTI + two NRTIs)

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BACKGROUND

Elsulfavirine (VM1500; ESV) is an oral pro-drug of VM1500A a novel, potent NNRTI with a unique clinical pharmacokinetic profile, very low toxicity and broad-spectrum activity across HIV-1 variants.
A 20 mg oral capsule formulation of ESV was approved in 2017 for treatment of HIV-1 in combination with two nucleoside reverse transcriptase inhibitors (NRTI) as part of a standard antiretroviral therapy (ART) regimen, under the brand name Elpida® in Russia and EAEU (Kazakhstan). ESV has been applied for marketing authorization in Thailand, Indonesia, and Colombia, and initiated a regulatory submission in China and is in development for once weekly, once monthly or less frequent dosing in US, European and Asian countries.
The Post-Authorization Study of Efficacy and Safety (PASS) was initiated in 19 clinical sites across Russia in 2018 to obtain safety and efficacy data from HIV-1 infected patients treated with Elpida in combination with two NRTIs.

MATERIAL AND METHODS

This analysis presents interim results of the PASS study with the cut-off date of March 30, 2020. The enrolled population includes both HIV-1-infected patients who receive 20 mg ESV daily as part of their first line ART regimen and patients switched from previous ART

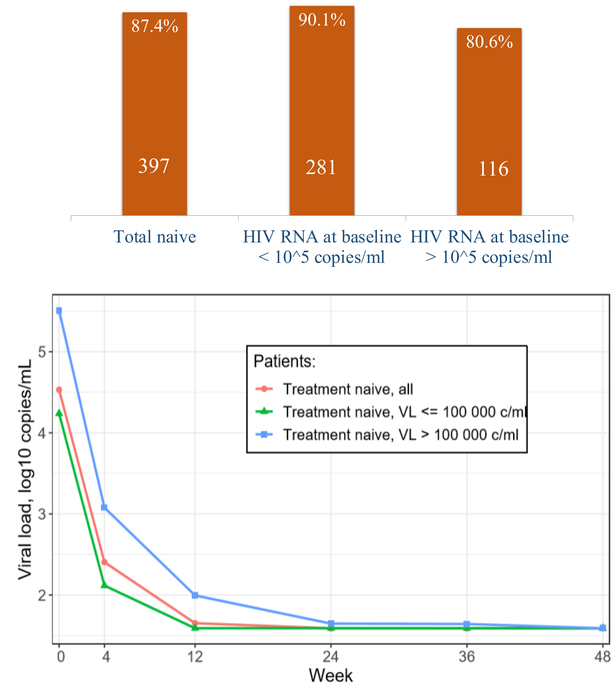
Inclusion criteria:
1. Signed Patient Information Sheet and Informed Consent Form.
2. Men and women aged ≥ 18 years.
3. Confirmed HIV-1 infection.
4. Patients prescribed first line Elpida-based ART including ART-naive patients or switched to Elpida from another first line ART regimen due to intolerance (transfer from other NNRTIs — inside the class; transfer from protease inhibitors, including boosted ones, due to lipid metabolism disorders or other adverse events (AEs) if the virological effectiveness of the previous ART regimen reached undetectable levels of viral load).

Efficacy of therapy was analyzed for treatment-naïve patients. Efficacy endpoints include viral load, CD4+ T cell count, and drug resistance. Safety endpoints include clinical AEs), serious adverse events (SAEs), ECG and laboratory data.

RESULTS

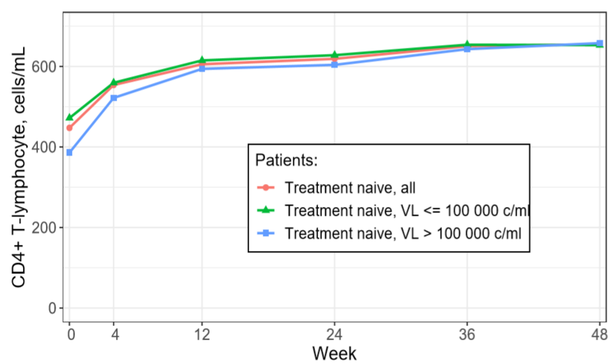
397 treatment-naïve patients completed 48 weeks or Elpida-based therapy, of which 281 patients had a baseline viral load of ≤ 10^5 c/mL, while 116 patients had a baseline viral load of > 10^5 c/mL. A significant reduction in viral load from baseline was observed from Week 4 and it was sustained through 48 weeks of treatment in this sub-population of patients.
In the sub-population of patients with baseline viral load of ≤ 10^5 copies/mL the viral load decreased by at least 1 Log_{10} at Week 4 in 249 (88.6%) patients, and in 108 (93.1%) patients on sub-population of patients with baseline viral load of >10^5 copies/mL. At Week 48, 87.1% of treatment-naïve patients had an undetectable viral load (Figure 1).

Figure 1. Efficacy overview: Viral load; MITT sub-population of treatment-naïve patients completing 48 weeks. N = 397



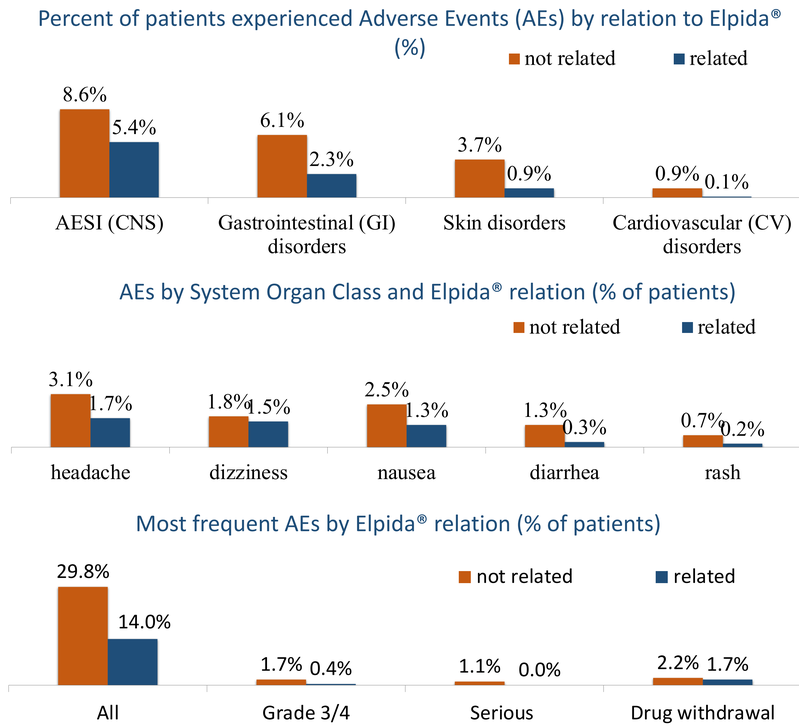
A significant immunological response was achieved at Week 4 and was sustained through 48 weeks of treatment.
The CD4+ T cell count increased from 415 to 595 c/ml, independent of the baseline viral load (Figure 2).

Figure 2. Efficacy overview; CD4+ count; MITT sub-population: naïve patients completing 48 weeks. N = 397



The treatment was well tolerated. Most of the observed AEs were of mild/moderate severity (Figure 3).
A subgroup of 131 patients completed 96 weeks of treatment confirming sustained efficacy and no significant safety issues.

Figure 3. PASS Interim Analysis: 48 weeks cut-off. Favorable Safety Profile. Safety population: patients completed 48 weeks. N = 1015



12 (1.1%) patients reported SAEs, all deemed unrelated to study treatment (Table 1).

Table 1. SAEs by relation to Elpida.
Safety population: patients completed 48 weeks. N = 1015

N=1015	Not related	Related
Number (%) of patients	8 (0.8%)	0
Naïve N=397	5 (1.3%) Acute HCV; Cystitis; Pneumonia; Comminuted fracture Spinal column injury; Spinal cord injury; Aspartate aminotransferase increased; Cervix carcinoma; Hodgkin's disease	0
Experienced N=618	3 (0.5%) Respiratory tract infection; Carbon monoxide poisoning; Weight decreased	0

CONCLUSIONS

The interim analysis of the PASS study supports the previous safety and efficacy data from earlier clinical studies of Elpida and encourages further treatment with this new NNRTI. The preliminary efficacy data shows a consistently high proportion of viral suppression in patients with significant immunological efficacy. The safety and tolerability profile is favorable and allows for high adherence and long-term treatment with ESV 20 mg as part of ART.